AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

1. (Currently amended) A method of producing a templated extracellular matrix, comprising the steps of: providing a nanostructured artificial template; **[[and]]** contacting the nanostructured artificial template with a population of cells**; culturing the population of cells to produce** ~~activated for producing~~ a templated extracellular matrix.

2. (Currently amended) The method of claim 1, where**in** the artificial template comprises a biocompatible ~~texture~~ **textured** surface.

3. (Currently amended) The method of claim 1, wherein the artificial template comprises one of aligned polymer, etched silicon, textured polymers, etched semi-conductor material, and glass.

4. (Currently amended) The method of claim 1, wherein the templated extracellular matrix is used for generating one of corneal stroma and **[[other]]** structured connective **tissues, including** ~~tissue such as~~ a ligament, a tendon, a fascia and annulus fibrosis.

5. (Currently amended) A method of producing a templated extracellular matrix, comprising the steps of: **providing a solution of a monomer or a polymeric sub-units;** controlling **[[a]]** flow of **[[a]]** **the** ~~polymer~~ solution into a device having a substrate, **wherein** the device **generates** ~~generating~~ a shear flow **in the solution induced by relative motion of the substrate to the solution; controlling the solution conditions to allow polymerization of the monomers or the polymeric sub-units; inducing alignment of the monomers by the shear flow to form polymeric structures in the direction of the flow field** ~~to induce alignment of polymer structures~~; controlling a plurality of parameters during **the**

polymerization; generating a ~~first~~ layer of nanostructured artificial template **composed of the aligned polymers**; contacting the ~~first~~ layer of nanostructured artificial template with a ~~first~~ population of cells; and maintaining the nanostructured artificial template and the ~~first~~ population of cells in a culture**, thereby producing** the ~~to produce a~~ templated extracellular matrix.

6. (Currently amended) The method of claim 5, wherein the polymer is a biopolymer**,** **including a** ~~such as~~ collagen.

7. (Currently amended) The method of claim **5** ~~6, wherein the method~~ further **comprising** ~~comprises~~ the steps of: mixing a solution of collagen **sub-units** with phosphate buffered saline solution; adjusting the pH of the solution to 7.4±0.2 to **promote polymerization or self-assembly of the collagen sub-units into collagen fibrils of controlled diameter**; applying the solution at a controlled rate onto a substrate which generates a shearing flow **by relative motion of the solution to the substrate**; causing preferential orientation of the self-assembling collagen fibrils; and **repeating the steps to generate** ~~generating~~ successive layers, **wherein** each layer **represents** ~~representing~~ a portion of the ~~component~~ **final assembled structure**.

8. (Currently amended) The method of claim 7, wherein the layers have a uniform, controllable thickness ranging from ~~sub-micron~~ **about 1 nanometer** to **about** 100 microns.

9. (Original) The method of claim 6, wherein the collagen is type I and/or type V collagen.

10. (Currently amended) The method of claim **[[5]]** **7**, wherein the principle orientation of the aligned fibrils in a single layer alternates in each successive layer.

11. (Currently amended) The method of claim 7, wherein the angle between the principle orientation of each layer is approximately in the range of 0 **(parallel)** to 180 degrees.

12. (Original) The method of claim 5, wherein the solution properties, including temperature, concentration and surfactant composition are controlled.

13. (Currently amended) The method of claim 5, wherein the shear flow is generated by spinning the substrate at a controlled rate in a range of approximately 50 to 50,000 **[[Hz]]** **revolutions per second**.

14. (Original) The method of claim 5, wherein the shear flow is generated by drawing the substrate out of the collagen solution.

15. (Currently amended) The method of claim 5, wherein **[[the]]** atmosphere **surrounding the substrate** is controlled to a specified temperature and relative humidity.

16. (Currently amended) The method of claim 5, wherein the solution conditions are modulated to control the polymerization kinetics ~~and morphology~~ **of the monomer or polymer sub-unit solution and final morphology of the polymerized polymer in the structured layer**.

17. (Currently amended) The method of claim 5, wherein the use of shear flow aligns **the** polymerizing polymer chains in a layer such that **the polymerized** polymers are predominantly aligned parallel to each other.

18. (Currently amended) The method of claim 5, further comprising angular rotation of the substrate **around a center point to provide** ~~providing~~ shear flow **in a thin**

liquid layer due to centripetal forces which confines and orients the polymerizing monomers or polymeric sub-units ~~and confinement to orient the polymerized polymers~~.

19. (Currently amended) The method of claim **5** ~~[[18]]~~, wherein **the shear flow rate is a combined result of** an input flow rate, solution viscosity and substrate rotational velocity**, which produces** ~~combine to produce~~ a shear rate between 1 s^{-1} and 500,000 s^{-1}.

20. (Currently amended) The method of claim **5** ~~[[18]]~~, wherein **the shear flow rate is a combined result of** an input flow rate, solution viscosity and substrate rotational velocity**, which produces** ~~combine to produce~~ a shear rate ~~preferably~~ between the range 10 s^{-1} and 10,000 s^{-1}.

21. (Currently amended) The method of claim ~~[[5]]~~ **7**, wherein an additional layer comprising collagen type IV and cell adhesion proteins such as, laminin, fibronectin and/or any integrin receptor is deposited between or onto **the** aligned polymer layers.

22. (Currently amended) The method of claim ~~[[5]]~~ **7**, wherein a construct of a plurality of aligned layers is used as a replacement or repair of the human corneal stroma.

23. (Currently amended) The method of claim 7, wherein the alignment of the polymers in a plane of second and subsequent layers is predominantly parallel with the alignment of the polymers in a plane of the ~~first~~ **preceding** layer.

24. (Currently amended) The method of claim 7, wherein the alignment of the polymers in a plane of a layer in a second and subsequent layers is predominantly orthogonal with the alignment of the polymers in the plane of the ~~first~~ **preceding** layer.

25. (Currently amended) The method of claim 7, wherein the alignment of the polymers

in a plane of a layer in the second and subsequent layers does not have a defined angular relationship to the alignment of the polymers in a plane the ~~first~~ **preceding** layer.

26. (Original) The method of claim 5, wherein the monomer is included in an aqueous solution.

27. (Currently amended) The method of claim 26, wherein the monomer is **a** collagen **sub-unit**.

28. (Currently amended) The method of claim 26, wherein the monomer is extracted or recombinant collagen **sub-unit**.

29. (Currently amended) The method of claim 27, wherein the collagen **monomer** is Type I **[[as]] in** the polymerizing medium.

30. (Original) The method of claim 27, wherein the collagen is Type I and Type V to assist in creation of heterotypic fibrils.

31. (Currently amended) The method of claim 5, wherein the ~~polymer~~ **monomer** solution is ~~injected~~ **provided** at a constant **flow** rate.

32. (Currently amended) The method of claim 5, wherein the ~~polymer~~ **monomer** solution is ~~injected~~ **provided** with a flow rate between 0.05-1000 ml/min.

33. (Currently amended) The method of claim 5, wherein the ~~material~~ **monomer solution** is ~~preferably injected~~ **provided** with a flow rate between of 0.1-100.0 ml/min.

34. (Currently amended) The method of claim 5, further comprising a ~~post-processing~~ step ~~including spinning off any effluent material from the substrate~~ **of removing**

any excess, unpolymerized solution from the substrate.

35. (Currently amended) The method of claim 5, further comprising ~~the substrate and~~ a substrate holder being modified to minimize waste of polymerization solution **by guiding or channeling the flow of the monomer solution into a restricted area on the substrate**.

36. (Currently amended) The method of claim 5, wherein the solution is ~~preferably~~ composed of 8:1:1 ratio of **3 mg/ml** collagen type I **in deionized water** ~~(3 mg/ml)~~ to 10xPBS to 0.1M NaOH with pH adjusted to 7.4.

37. (Currently amended) The method of claim 5, wherein **[[the]]** viscosity of the solution is between 1 mPa.s and 100 Pa.s.

38. (Currently amended) The method of claim 5, where**in [[the]]** viscosity **of the** solution is ~~preferably~~ between 5 mPa.s and 1 Pa.s.

39. (Original) The method of claim 5, wherein the substrate comprises one of a flat surface or curved surface.

40. (Original) The method of claim 39, wherein the flat surface is optically smooth.

41. (Currently amended) The method of claim 39, wherein ~~preferably~~ the flat surface has a surface roughness of approximately ~~less than~~ **between 1 and** 10 microns.

42. (Original) The method of claim 39, wherein the substrate is a borosilicate glass disk.

43. (Currently amended) The method of claim 5, wherein a surface of the substrate is treated to control adhesion of the polymer **to the substrate** and **the** wetting of the solution **on the substrate**.

44. (Currently amended) The method of claim 5, wherein a surface of the substrate is ultrasonicated in ~~10% micro 90 (Brand)~~ **a surfactant** cleaner for a time duration.

45. (Original) The method of claim 5, wherein a surface of the substrate is plasma cleaned.

46. (Original) The method of claim 5, wherein a surface of the substrate is homogeneous.

47. (Original) The method of claim 5, wherein the substrate has a surface treatment that is heterogeneous.

48. (Original) The method of claim 5, wherein the substrate has a surface treatment that is patterned.

49. (Currently amended) The method of claim 5, wherein **[[a]]** **the** substrate is patterned to constrain the flow **of the solution to a part of the substrate**.

50. (Currently amended) The method of claim **[[5]]** **6**, wherein **the parameters controlled are the** **[[a]]** surface **chemistry and morphology** of the substrate and **the** atmospheric conditions ~~are modulated~~ to control self-assembly **of the collagen monomers**.

51. (Currently amended) The method of claim 5, wherein **one or more** additives are ~~injected~~ **mixed** with the ~~polymer~~ **monomer** solution to control the polymerization process and **the** final morphology of the **polymerized** layer.

52. (Currently amended) The method of claim 51, wherein the additives **can be one or more** **[[are]]** proteoglycans.

53. (Currently amended) The method of claim **[[51]]** **52**, wherein the **additive is** ~~additives are~~ at least one of chondroitin sulfate, dermatan sulfate and keratan sulfate proteoglycans.

54. (Currently amended) The method of claim **[[51]]** **52**, wherein the proteoglycan**[[s]]** **is** ~~are one of~~ at least **one** ~~or a combination~~ of decorin, lumican, biglycan, keratocan **[[or]]** **and** syndican.

55. (Currently amended) The method of claim **[[51]]** **52**, wherein the percent (by weight) of added proteoglycan**[[s]]** is between 0.25**%** and 50.0**%**.

56. (Currently amended) The method of claim **[[51]]** **52**, wherein the percent by weight of added proteoglycan**[[s]]** is between 0.5**%** and 10**%**.

57. (Currently amended) A method of producing a templated extracellular matrix **layers**, comprising the steps of: providing a nanostructured artificial template; contacting the nanostructured artificial template with a ~~first~~ population of cells; and maintaining the nanostructured artificial template and the ~~first~~ population of cells in ~~culture~~ **conditions sufficient to promote generation by the cells of further extracellular matrix** to produce a templated extracellular matrix having a **layer of extracellular matrix possessing a** first surface and a second surface.

58. (Currently amended) The method of claim 57, further comprising the step of stacking a plurality of templated extracellular matrix layers oriented at any arbitrary angle with respect to each other to form a multilaminar templated extracellular matrix having a first surface and a second surface**, thereby producing a plurality of templated extracellular matrix layers**.

59. (Currently amended) The method of claim 58, wherein the multilaminar templated extracellular matrix layer is a biomimetic corneal stroma.

60. (Original) The method of claim 58, further comprising the steps of: contacting the first surface of the multilaminar templated extracellular matrix with a second population of cells; and maintaining the multilaminar templated extracellular matrix and the second population of cells in culture to produce a multilaminar templated extracellular matrix having layer of the second population of cells on the first surface.

61. (Original) The method of claim 60, further comprising the steps of: contacting the second surface of the multilaminar templated extracellular matrix with a third population of cells; and maintaining the multilaminar templated extracellular matrix and the third population of cells in culture to produce a multilaminar templated extracellular matrix having layer of the third population of cells on the second surface.

62. (Original) The method of claim 57 wherein the cells are mammalian cells.

63. (Original) The method of claim 57 wherein the cells are mammalian fibroblasts.

64. (Original) The method of claim 60 wherein the cells are mammalian cells.

65. (Original) The method of claim 60 wherein the cells are corneal epithelial cells.

66. (Currently amended) The method of claim 63, wherein the mammalian fibroblasts are activated by treatment with **at least one of** ascorbic acid, pharmacologically acceptable organic and inorganic ascorbate salts and ascorbate esters.

67. (Currently amended) The method of claim 66, wherein the activated fibroblasts are made quiescent by the ~~remote~~ **removal** of ascorbate.

68. (Original) The method of claim 61 wherein the cells are mammalian cells.

69. (Original) The method of claim 61 wherein the cells are corneal endothelial cells.

70. (Currently amended) The method of claim 57, wherein the nanostructured artificial template ~~is unstressed~~ **has no mechanical load placed upon it while the cells generate further extracellular matrix**.

71. (Currently amended) The method of claim 57, wherein the nanostructured artificial template is subjected to **a** tensile stress **while the cells generate further extracellular matrix**.

72. (Currently amended) The method of claim 60 wherein the multilaminar templated extracellular matrix ~~is unstressed~~ **has no mechanical load placed upon it while the cells generate further extracellular matrix**.

73. (Currently amended) The method of claim 60 wherein the multilaminar templated extracellular matrix is subjected to tensile stress **while the cells generate further extracellular matrix**.

74. (Currently amended) The method of claim 61 wherein the templated extracellular matrix ~~is unstressed~~ **has no mechanical load placed upon it while the cells generate further extracellular matrix**.

75. (Currently amended) The method of claim 61, wherein the templated extracellular matrix is subjected to tensile stress **while the cells generate further extracellular matrix**.

76. (Currently amended) The method of claim 57, wherein the nanostructured artificial

template comprises collagen.

77. (Currently amended) The method of claim 76, wherein the nanostructured artificial template further comprises proteoglycan**[[s]]**.

78. (Original) The method of claim 76, wherein the nanostructured artificial template further comprises at least one of chondroitin sulfate, dermatan sulfate and keratan sulfate proteoglycans.

79. (Currently amended) The method of claim **[[76]]** **77**, wherein the proteoglycan**[[s are]]** **is** ~~**one of**~~ at least ~~**or a combination**~~ **one** of decorin, lumican, biglycan, keratocan [[or]] **and** syndican.

80. (Currently amended) The method of claim **[[76]]** **77**, wherein the percent (by weight) of proteoglycan**[[s]]** is between 0.25**%** and 50.0**%**.

81. (Withdrawn) A biomimetic corneal stroma produced by the steps of: providing a nanostructured artificial template; contacting the nanostructured artificial template with a first population of eukaryotic cells; maintaining the nanostructured artificial template and the first population of cell in culture to produce a templated extracellular matrix; repeating the steps of providing, contacting and maintaining to produce additional templated extracellular matrices; and stacking a plurality of templated extracellular matrices oriented at any arbitrary angle with respect to each other.

82. (Withdrawn) The biomimetic corneal stroma of claim 81 wherein the eukaryotic cells are mammalian fibroblasts.

83. (Withdrawn) The biomimetic corneal stroma of claim 81 wherein the eukaryotic cells are human keratocytes.

84. (Withdrawn) The biomimetic corneal stroma of claim 81 further comprising the step of treating the eukaryotic cells with an ascorbate compound selecting from the group consisting of ascorbate acid, pharmaceutically acceptable organic and inorganic salts of ascorbate, organic and inorganic esters of ascorbate and mixtures thereof.

85. (Withdrawn) The biomimetic corneal stroma of claim 84 further comprising the step of removing the ascorbate compound.

86. (Withdrawn) A biomimetic cornea produced by the steps of: providing a nanostructured artificial template; contacting the nanostructured artificial template with a first population of eukaryotic cell; maintaining the nanostructured artificial template with the eukaryotic cells to form a template extracellular matrix; repeating the steps of providing, contacting and maintaining to form additional templated extracellular matrices; stacking a plurality of templated extracellular matrices oriented at any arbitrary angle with respect to one another to form a multilaminar templated extracellular matrix; contacting a first surface of the multilaminar templated extracellular matrix with a second population of cells; and maintaining the multilaminar templated extracellular matrix in culture to form a biomimetic cornea.

87. (Withdrawn) A method of making a multilaminar nanostructured template comprising: introducing a monomer solution from a first inlet, between a polymer accepting surface and a polymer rejecting surface to first outlet to produce an aligned polymer layer; increasing the spacing between the polymer accepting surface and the polymer rejecting surface; introducing the monomer solution into a second inlet and recovering the monomer solution from a second outlet wherein the flow from the second inlet to the second outlet is substantially orthogonal to the flow from the first inlet to the first outlet; and producing an aligned polymer layer in which the polymer molecules are substantially orthogonal to the polymer molecules of the previous layer.

88. (Withdrawn) The method of claim 87 wherein the polymer is collagen.

89. (Withdrawn) The method of claim 87 wherein the polymer rejecting surface is cooled.

90. (Withdrawn) The method of claim 87 wherein the polymer accepting surface is heated.